Remarks

Claims 21-29 define a improved microarray screening method, wherein the primers are selected to bind to non-consensus sequence so that non-specific binding is minimized. Claims 34-40 are drawn to a method of screening a microarray of genes including the ***same*** regulatory sequence, i.e., regulatory-sequence based gene microarrays composed nucleic acid sequences of genes ***whose non-coding region contains the same defined nucleotide bases for enhancers or repressors to bind to; and genes whose protein products can bind to designated regulatory sequences***. There are many examples of such regulation occurring in cells, and promotion of a specific cellular event usually requires the concerted and coordinated activation of a group of genes. The claimed invention contrasts with the currently available DNA microarray technology which is based on screening the coding sequences of thousands of genes, many of which may only be "ESTs" of unknown function. The claimed technology is based on a specific subset of sequences from genes ***whose expressions are regulated by the same regulatory mode, i.e. the activation of gene expression based on the activation or deactivation of defined DNA sequences.***

Rejection Under 35 U.S.C. § 112, second paragraph

Claims 21-29 and 34-40 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Claims 21-29 are now drafted as "Jepson" type claims - acknowledging that microarrays and microarray screening is known, and emphasizing the improvement as the selection of the primers to avoid the non-specific bindings which is such a problem with existing microarray screening. Support is found in the application at page 3, lines 7-16; page 15, lines 15-21.

Rejection Under 35 U.S.C. § 102

Claims 22, 23, 25-29 and 34-38 were rejected under 35 U.S.C. § 102(b) as being anticipated by Nature Genetics 14(4):457-460 by DiRisi *et al.* ("DiRisi"). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

DiRisi teaches the assessment of mRNA levels in cell lines *via* the hybridization of cDNA probes generated from single oligo dT-selected mRNA pools (prepared from mRNA by oligo dT-primed polymerization; see Methods, page 459). DiRisi teaches nothing more than an extremely basic data mining technique. DeRisi teaches DNA microarrays, containing 1,161 total elements, including 870 different cDNAs and controls. However, DeRisi fails to teach or suggest primers as defined by claims 21-29 or a microarray in which all genes are under the control of the same regulatory element (i.e. having common regulatory sequences).

Claims 22, 24-28 and 34-37 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 6,524,800 to Lockhart *et al.* ("Lockhart"). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Lockhart teaches the characterization of cellular effects of potentially therapeutic compounds on a genome-wide scale by monitoring changes in messenger RNA levels in treated

cells with high density oligonucleotide probe arrays (see abstract). Lockhart is a perfect example of methods being used to screen thousands of coding sequences. As discussed above, results obtained from such large screens provide only a general sketch of which gene expressions are gained or lost in a specific physiological condition. Lockhart does not even teach a grouping of genes based upon their functional capability, such as cell proliferation, cell cycle apoptosis, DNA repair. Lockhart is in complete contrast to the methods by claims 34-40, wherein sequences from genes are grouped according to their regulatory modalities. There is no disclosure of the method using primers as defined by claims 21-29.

Rejection Under 35 U.S.C. § 103

Claims 39 and 40 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Nature Genetics 14(4):457-460 by DiRisi *et al.* ("DiRisi"). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

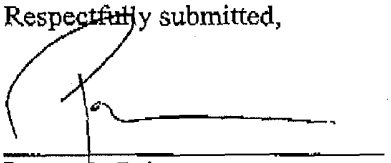
Claims 39 and 40 depend from method claim 34. Claim 34 relies upon, in part, the hybridization to sequences from genes whose expression is under the control of *the same regulatory element.* There is nothing in DiRisi that would lead one to a method using a microarray in which there is a common regulatory element. In fact DiRisi, representative of the prior art in general, teaches combinations of genes other than based on the inclusion of a specific regulatory agent.

In summary, none of the cited art recognizes how one can design the primers to minimize non-specific binding in a method for screening of a microarray, as defined by claims 21-29.

None of the art recognizes the usefulness of combining genes under the control of the same regulatory agent. The law is well established - failure to disclose the claimed elements precludes a rejection under 35 U.S.C. 102; failure to disclose the motivation to modify and/or combine, as applicants have done, with a reasonable expectation of success, precludes a rejection under 35 U.S.C. 103.

Allowance of claims 21-29 and 34-40 is respectfully solicited.

Respectfully submitted,



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